chapter

11 Blood and the Immune System

In this chapter

- Exploration: Tracing an Infection
- Investigation 11.1: Diagnosing Disease by Examining Blood Cells
- Web Activity: Blood Typing
- Mini Investigation: Observing Phagocytosis
- Case Study: Bovine Spongiform Encephalopathy
- Web Activity: Virtual Immunology Laboratory
- Explore an Issue: The Future of Stem Cell Research

To appreciate the importance of the immune system, consider severe combined immunodeficiency (SCID), also known as the "boy in the plastic bubble" syndrome after David Vetter, an American boy who had to live in a sterile plastic bubble. SCID is a rare disease of the immune system, and those affected must live in a virtually germ-free environment or risk contracting life-threatening infections. In 2006, a baby in Ontario was born with SCID. Treatments for SCID include bone marrow transplants and gene therapy.

Unlike familiar infectious diseases caused by viruses and bacteria, bovine spongiform encephalopathy (BSE) is caused by a neurological invader that does not contain nucleic acids. The disease is caused by a *prion*, an abnormal infectious version of a protein. During the 1980s and early 1990s, thousands of people in Britain ate beef from cattle that had BSE, often called mad cow disease (**Figure 1**). By the mid-1990s, the human version of mad cow disease, known as variant Creutzfeldt–Jakob disease, surfaced, and scientists considered the possibility that the disease could be transmitted from cows to people through the food chain.

STARTING points

Answer these questions as best you can with your current knowledge. Then, using the concepts and skills you have learned, you will revise your answers at the end of the chapter.

1. How do you think the idea that a protein can cause an infectious disease has altered the way we think about disease?
2. Which of the following medical conditions have been linked with bacteria, viruses, or prions?
   (a) heart attack
   (b) ulcers
   (c) AIDS
   (d) measles
   (e) diabetes mellitus
3. Allergies are caused by an over-reaction of your immune system. Harmless agents, such as proteins in peanut butter, are recognized as harmful invaders and an immune response is mobilized. What other mistakes of the immune system can cause problems?

Career Connections:
Medical Laboratory Technologist; Pathologist

Figure 1
A prion causes BSE in cattle.

Exploration — Tracing an Infection

In this activity, you will simulate the spread of an infection. Each member of your class will be provided with a numbered plastic cup filled with a mystery fluid. One of these cups will contain an "infection."

Safety goggles and a lab apron must be worn for the entire laboratory.

Materials: index card, pen or pencil, numbered plastic cup of mystery fluid, dropper bottle of phenolphthalein indicator

- Write your name and cup number on your index card.
- Share your mystery fluid with a classmate. Pour all of your fluid into your partner's cup. Then, have your partner pour half of the combined fluids back into your cup. Both you and your partner then record the other person's cup number on your index card.
- Repeat the previous step until you have shared fluids with exactly three other students. Note that every class member will share fluids with three other students.
- Once all exchanges have occurred, your teacher will add a drop of phenolphthalein indicator to each of the cups. A pink colour indicates an infection.

(a) Can you identify the origin of the infection?
(b) If so, then identify the source. If not, why not?

11.1 Components of Blood

DID YOU KNOW ?

Water Content of Blood

Blood is not the most watery tissue of your body. It has been estimated that the grey matter of your brain is 85 % water.

plasma the fluid portion of the blood

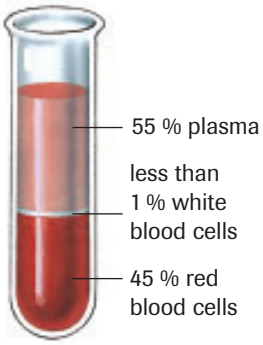


Figure 1
Proportions of fluid and cells in blood

The average 70-kg individual is nourished and protected by about 5 L of blood. Approximately 55 % of the blood is fluid; the remaining 45 % is composed of blood cells (**Figure 1**). All blood cells are produced by the bone marrow (**Figure 2**). The percentage of red blood cells in the blood is called the hematocrit. The fluid portion of the blood is referred to as the **plasma**, which is about 90 % water, allowing it to be described as a fluid tissue. As in other tissues, the individual cells in the blood work together for a common purpose.

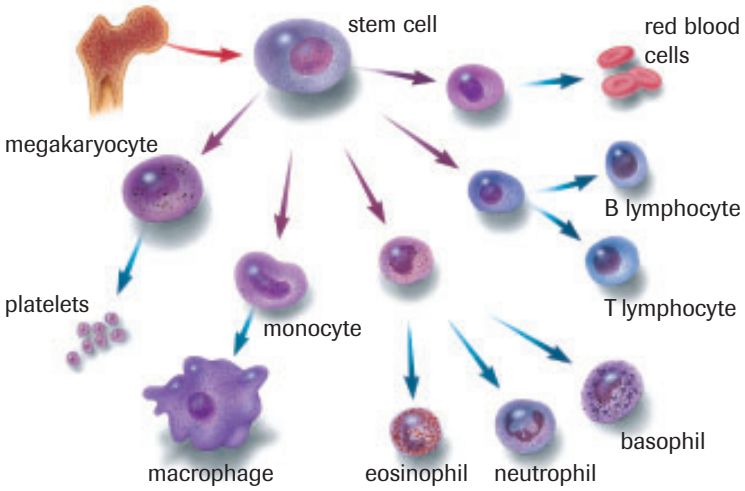


Figure 2
Stem cells of the bone marrow give rise to blood cells. The agranulocytes include the monocytes and lymphocytes. The granulocytes include the eosinophils, basophils, and neutrophils.

The plasma also contains blood proteins, glucose, vitamins, minerals, dissolved gases, and waste products of cellular metabolism. The large plasma proteins help maintain homeostasis. One group of proteins is called the albumins; they, along with inorganic minerals, establish an osmotic pressure that draws water back into capillaries and helps maintain body fluid levels. A second group of proteins, the globulins, help provide protection against invading microbes. Fibrinogens, the third group of proteins, are important in blood clotting. **Table 1** summarizes the types of plasma proteins and their functions.

Table 1 Plasma Proteins

Type	Function
albumins	osmotic balance
globulins	antibodies, immunity
fibrinogens	blood clotting

Erythrocytes

erythrocyte a red blood cell that contains hemoglobin and carries oxygen

The primary function of **erythrocytes**, red blood cells, is the transport of oxygen. Although some oxygen diffuses into the plasma, the presence of hemoglobin increases the ability of the blood to carry oxygen by a factor of almost 70. Without hemoglobin, your red blood cells would supply only enough oxygen to maintain life for approximately 4.5 s. With hemoglobin, humans can survive without oxygen for a few minutes. This is not much time, but remember that the blood returns to the heart and is pumped to the lungs, where oxygen supplies are continuously replenished. This might indicate why people survive even when the heart stops for short periods of time. Children who have been immersed in cold water for longer than a few minutes have survived with comparatively minor cell damage because colder temperatures slow body metabolism and decrease oxygen demand.

An estimated 280 million hemoglobin molecules are found in a single red blood cell. The hemoglobin is composed of heme, the iron-containing pigment, and globin, the protein structure. Four heme groups, each containing an iron atom, attach to the folded protein structure and bind with oxygen molecules. The oxyhemoglobin complex gives blood its red colour. Once oxygen is given up to cells of the body, the shape of the hemoglobin molecule changes, causing the reflection of blue light. This explains why blood appears blue in the veins.

Red blood cells are biconcave (concave on both sides) disks approximately 7 μm in diameter. This shape provides a greater surface area for gas exchange—between 20 % and 30 % more surface area than a sphere. The outer membranes of red blood cells become brittle with age, causing them to rupture as they file through the narrow capillaries. Since red blood cells live only about 120 days, cell reproduction is essential. One estimate suggests that at least five million red blood cells are produced every minute of the day.

Red blood cells do not contain a nucleus when mature, which allows more room for the cell to carry hemoglobin. This enucleated condition raises two important questions. First, since cells, by definition, contain a nucleus or nuclear material, are red blood cells actually cells? The second question addresses cell reproduction: how do cells without a nucleus and chromosomes reproduce? The answer to both of the above questions can be found in bone marrow, where red blood cells are produced by nucleated stem cells. The young cells lose their nuclei as they are discharged into the bloodstream.

The average male has about 5.5 billion red blood cells per millilitre of blood, while the average female has about 4.5 billion. Individuals living at high altitudes can have red cell counts as high as 8 billion per millilitre. How does the body ensure that adequate numbers of red blood cells are maintained? Specialized white blood cells, located primarily in the spleen and liver, monitor the age of red blood cells and remove debris from the circulatory system. Following the breakdown of red blood cells, the hemoglobin is released. Iron is recovered and stored in the liver and bone marrow for production of new red blood cells. The heme is transformed into bile pigments.

A deficiency in hemoglobin or red blood cells decreases oxygen delivery to the tissues. This condition, known as **anemia**, is characterized by low energy levels. The most common cause of a low red blood cell count is hemorrhage. Physical injury, bleeding due to ulcers, or hemorrhage in the lungs due to tuberculosis can cause anemia. If more than 40 % of the blood is lost, the body is incapable of coping. Anemia may also be associated with a dietary deficiency of iron, which is an important component of hemoglobin. The red blood cells must be packed with sufficient numbers of hemoglobin molecules to ensure adequate oxygen delivery. Raisins and liver are two foods rich in iron.

DID YOU KNOW?

Colour of Blood

The word *erythrocyte* comes from the Greek *erythros*, meaning "red." However, a single red blood cell does not appear red but pale orange—the composite of many red blood cells produces the red colour.

DID YOU KNOW?

How Old Is Your Blood?

Because red blood cells live only 120 days, they are continually breaking down and being replenished. The misconception that "young blood" is better than "old blood" persists even today. The blood of elderly people is virtually the same as the blood of young people.

anemia the reduction in blood oxygen due to low levels of hemoglobin or poor red blood cell production

Leukocytes

White blood cells, or **leukocytes**, are much less numerous than red blood cells. It has been estimated that red blood cells outnumber white blood cells by a ratio of 700 to 1. White blood cells have a nucleus, making them easily distinguishable from red blood cells. In fact, the shape and size of the nucleus, along with the granules in the cytoplasm, have been used to identify different types of leukocytes (**Figure 2**, previous page). The granulocytes are classified according to small granules in the cytoplasm that become visible when stained. The agranulocytes are white blood cells that do not have granules in their cytoplasm. Granulocytes and agranulocytes are both produced in the bone marrow, but agranulocytes are modified in the lymph nodes. The function of some leukocytes is to destroy invading microbes by phagocytosis; they squeeze out of capillaries and move toward the microbe like an amoeba. Once the microbe has been engulfed, the leukocyte releases enzymes that digest the microbe and the leukocyte itself. The function of other white blood cells is to form special proteins, called antibodies, which interfere with invading microbes and toxins.

leukocyte a white blood cell

DID YOU KNOW?

Average Blood Volume

The average male contains an estimated 80 mL of blood for every kilogram of body mass. The average female contains an estimated 65 mL of blood for every kilogram of body mass.

INVESTIGATION 11.1 ***Introduction***

Diagnosing Disease by Examining Blood Cells

White blood cells often provide physicians with information used in diagnosing disease. In this investigation, you will examine and count different types of white blood cells, then relate this information to disease diagnosis.

To perform this investigation, turn to page 369.

Report Checklist

- Purpose
- Problem
- Hypothesis
- Prediction
- Design
- Materials
- Procedure
- Evidence
- Analysis
- Evaluation
- Synthesis

platelet a component of blood responsible for initiating blood clotting

Platelets

Platelets, or thrombocytes, do not contain a nucleus and are produced from large nucleated cells in the bone marrow. Small fragments of cytoplasm break from the large megakaryocyte, a large cell in the bone marrow, to form platelets. Platelets play an important role in blood clotting. When a blood vessel is damaged, the cells of the vessel wall release a substance that makes them sticky, and platelets begin to stick to the injured site. As the platelets build up, they form a plug to stop the bleeding. The platelets change shape from round to spiny, and they release substances that trap more platelets and cause clotting proteins to form.

Practice

1. Name the two major components of blood.
2. List three plasma proteins and indicate the function of each.
3. What is the function of hemoglobin?
4. List factors that initiate red blood cell production.
5. What is anemia?
6. What is the role of platelets?

Blood Clotting

Blood clotting maintains equilibrium by preventing the loss of blood from torn or ruptured blood vessels. Blood clots also forestall the rupture of weakened blood vessels by providing additional support.

Trillions of platelets move through the blood vessels. When a blood vessel is damaged, platelets are activated and clump together to form a plug to stop the bleeding. The platelets release a protein called thromboplastin (**Figure 3**).

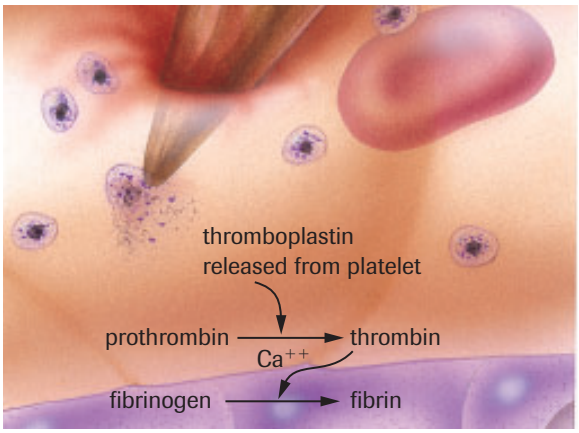


Figure 3
The thromboplastin released from the platelet initiates a series of reactions that produce a blood clot.

The thromboplastin, along with calcium ions present in the blood, activates a plasma protein called prothrombin. Prothrombin, along with another plasma protein, called fibrinogen, is produced by the liver. Under the influence of thromboplastin, prothrombin is transformed into thrombin. In turn, thrombin acts as an enzyme by splicing two amino acids from the fibrinogen molecule. Fibrinogen is converted into fibrin threads, which wrap around the damaged area, trapping red blood cells and more platelets to form a clot and stop bleeding (**Figure 4**).

Although blood clotting preserves life, it can also result in life-threatening situations. A **thrombus** is a blood clot that blocks a blood vessel. Because blood will not pass through the area, local tissues are not supplied with oxygen and nutrients. If a clot forms in the brain, cerebral thrombosis can cause a stroke. Coronary thrombosis—a clot in a coronary artery of the heart—can be equally dangerous.

Should a blood clot dislodge, it becomes an **embolus**. The embolus may travel through the body to lodge in a vital organ. Cerebral embolisms, coronary embolisms, and pulmonary embolisms can be life-threatening. What causes an embolus or thrombus is not completely understood, but scientists believe that genetic factors may be involved. It is known, however, that the incidence of thrombi and emboli increases as people get older.

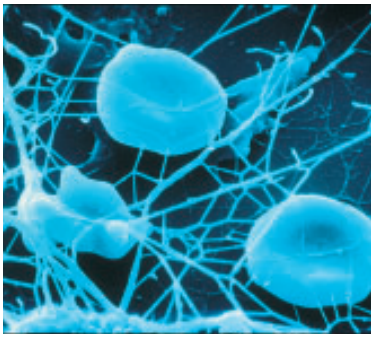


Figure 4
Formation of a blood clot. Red blood cells are caught in a mesh of fibrin.

thrombus a blood clot that forms within a blood vessel and blocks it

embolus a blood clot that dislodges and is carried by the circulatory system to another part of the body

Artificial Blood

On March 1, 1982, a precedent-setting legal case brought attention to an emerging medical technology. A man and woman, trying to push their car, were critically injured when they were hit by another car. For personal reasons, the couple chose not to have a blood transfusion. During the legal dispute that ensued, the wife died, and the courts ruled that action must be taken to save the husband's life. Five litres of fluosol—artificial blood—were transfused into the man over a period of five days. Doctors believed that the artificial blood could maintain adequate oxygen levels until the man's bone marrow began replenishing red blood cells.

Fluosol, a non-toxic liquid that contains fluorine, was developed in Japan. Fluosol carries both oxygen and carbon dioxide. It requires no blood matching, and when frozen, can be stored for long periods of time. Artificial blood, unlike human blood, does not have to undergo expensive screening procedures before being used in transfusions. Artificial blood will not carry human immunodeficiency virus (HIV), hepatitis, or any other virus. However, despite its advantages, artificial blood is not as good as the real thing. Although it carries oxygen, it is ill-suited for many of the other functions associated with blood, such as blood clotting and immunity. The real value of artificial blood is that it provides time until human blood can be administered. It could also serve as a supplement for patients with diseases like thalassemia (Cooley's anemia) or aplastic anemia, which require the patients to undergo multiple transfusions.

CAREER CONNECTION

Medical Laboratory Technologist

One of the many duties medical laboratory technologists (MLTs) perform is drawing blood for analysis. They also conduct routine lab tests and set up, clean, and maintain lab equipment. Survey Web sites for job opportunities for MLTs. Report on your findings.

www.science.nelson.com GO

ABO Blood Groups

In the 17th century, Jean-Baptiste Denis performed the first blood transfusion by injecting lamb's blood into a young boy. The youth survived, but a repeat of the experiment, on an older man, proved disastrous—the man died almost immediately. Denis attempted to explain what went wrong, but he lacked crucial information. Why do some transfusions help, while others kill?

At the turn of the 20th century, Karl Landsteiner discovered that different blood types exist. Therefore, the secret to successful transfusion was the correct matching of blood types. Markers called glycoproteins are located on the membrane of some of the red blood cells. Individuals with blood type A have a glycoprotein, the A marker, attached to their cell membrane. Individuals with blood type B have a glycoprotein, the B marker,

antigen a substance, usually protein, that stimulates the formation of an antibody

antibody a protein formed within the blood that reacts with an antigen

attached to their cell membrane. Individuals with blood type AB have both A and B markers attached to their cell membrane. Blood type O has neither marker.

Should an individual with blood type O receive blood from an individual with blood type A, the type O blood would recognize the A marker as a foreign invader (**Figure 5**). The A marker acts as an **antigen** in the body of the individual with blood type O. Special proteins, called **antibodies**, are produced in response to a foreign invader. The antibodies attach to the antigen markers and cause the blood to clump. It is important to note that antigen A would not cause the same immune response if transfused into the body of an individual with blood type A. The marker associated with blood type A would not be a foreign invader because A-type antigens are found on that individual's red blood cells. **Table 2** summarizes the antigens and antibodies for the four ABO blood groups.

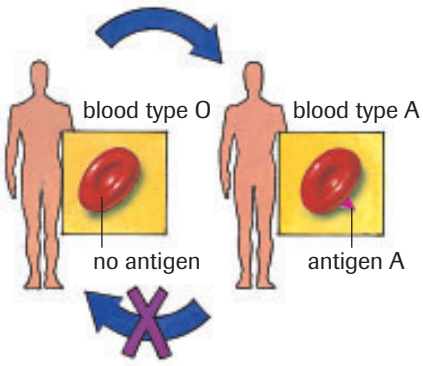


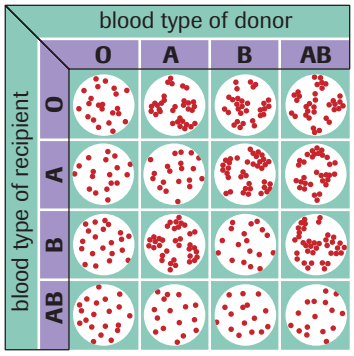
Figure 5
Individuals with blood type A can receive blood type O during a transfusion. However, individuals with blood type O cannot receive blood type A during a transfusion.

Table 2 Antigens and Antibodies Found in Blood Groups

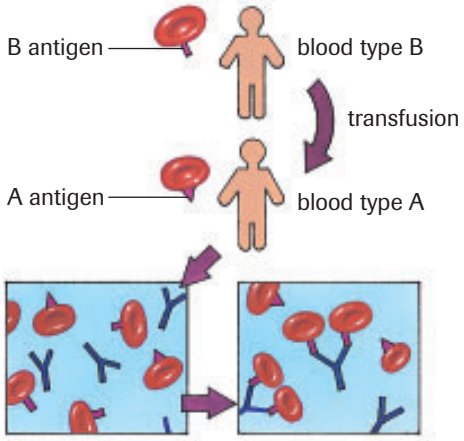
Blood group	Antigen on red blood cell	Antibody in serum
O	none	A and B
A	A	B
B	B	A
AB	A and B	none

The antibodies produced by the recipient act on the invading antigens. As shown in **Figure 6**, the antibodies cause **agglutination**, or clumping, of the blood. The importance of the correct transfusion is emphasized by the fact that agglutinated blood can no longer pass through the tiny capillaries. The agglutinated blood therefore clogs the capillaries and prevents the delivery of oxygen and nutrients. Individuals with type AB blood possess both antigens and, therefore, are able to receive blood from any donor. Blood type AB is the universal recipient. Blood type O is referred to as the universal donor because it can be donated to individuals of all blood types. Blood type O contains no antigen. Although antibodies will not be produced against type O, the immune system of individuals with blood type O can recognize antigens on other blood cells. Blood

agglutination the clumping of blood cells caused by antigens and antibodies



(a)



(b)

Figure 6
(a) Agglutination response of ABO blood groups
(b) Agglutination response of blood type A (recipient) to blood type B (donor)

type O, despite being the universal donor, may only accept blood from individuals with blood type O. Blood type AB, despite being the universal recipient, may only donate blood to individuals with blood type AB.

WEB Activity

Simulation—Blood Typing

Blood transfusions may be required during surgery or when a person loses blood due to trauma. Identifying a patient's blood type is critical to ensuring that the appropriate type of blood is provided. In this activity, you will follow an interactive animation in which you must identify the blood type of virtual patients and then give them a blood transfusion. You will also find additional information on the biology of blood types.

www.science.nelson.com GO

Rhesus Factor

During the 1940s scientists discovered another antigen on the red blood cell—the rhesus factor. Like the ABO blood groups, the rhesus factor is inherited. Individuals who have this antigen are said to be Rhesus positive (Rh+). Approximately 85 % of Canadians have the antigen. The remaining 15 % of individuals who do not have the antigen are said to be Rhesus negative (Rh–). Individuals who are Rh– may donate blood to Rh+ individuals, but should not receive Rh+ blood. The human body has no natural antibodies against Rh factors, but antibodies can be produced following a transfusion. Although Rh antibodies are produced in response to antigens, it should be pointed out that the immune reaction is subdued compared with that of the ABO group.

Rhesus-factor incompatibilities become important for Rh+ babies of Rh– mothers. If the baby inherits the Rh+ factor from the father, a condition called erythroblastosis fetalis can occur with the second and subsequent pregnancies. The first child is spared because the blood of the mother and baby are separated by the placenta (a membrane inside the uterus that exchanges materials between mother and baby). During birth, the placenta is shed from the uterus. Capillary beds rupture, and, for the first time, the blood of the baby comes into contact with the blood of the mother. The mother's immune system recognizes the Rh+ antigens and triggers the production of antibodies. But, by the time the antibodies are produced, the first baby is no longer connected to the placenta and has escaped the potentially dangerous situation. However, a second pregnancy presents problems if the fetus is Rh+. The mother retains many of the antibodies from her first encounter with Rh+ blood. If antibodies cross the placenta, they attach to the antigen on the red blood cells of the fetus, causing them to be destroyed. Symptoms of erythroblastosis fetalis include anemia, jaundice, and an enlarged liver.

SUMMARY *Components of Blood*

- Blood is composed mainly of plasma and blood cells.
- Plasma proteins play roles in maintaining homeostasis, in producing antibodies, and in blood clotting.

- Erythrocytes function primarily to transport oxygen.
  - Erythrocytes contain hemoglobin, which increases the amount of oxygen that can be carried in the blood.
  - Erythrocytes are produced in the bone marrow; once they leave, they have no nucleus and cannot reproduce.
- Leukocytes are an important part of the immune system.
- Platelets are cell fragments that clump together at the site of a damaged blood vessel to form a clot.
- Blood type A has the A antigen, type B has the B antigen, type AB has both, and type O has neither.
- Blood types must be matched before giving a blood transfusion.
  - An incompatible marker acts as an antigen in the recipient's body.
  - The recipient will produce antibodies against the antigen, causing agglutination.
  - AB is the universal recipient, and O is the universal donor.
- The Rhesus (Rh) factor is another potential source of blood incompatibility.

Section 11.1 Questions

1. What are erythrocytes and what is their primary function?
2. Explain the mechanism by which hemoglobin increases the ability of blood to carry oxygen.
3. Are erythrocytes true cells? Why or why not?
4. State two situations that result in a deficiency of hemoglobin.
5. How do white blood cells differ from red blood cells?
6. State two major functions associated with leukocytes.
7. How do platelets contribute to the formation of blood clots?
8. Differentiate between an embolus and a thrombus.
9. List the advantages and disadvantages associated with using artificial blood.
10. Cancer of the white blood cells is called leukemia. Like other cancers, leukemia is associated with rapid and uncontrolled cell production. Examine the test tubes shown in **Figure 7** and predict which subject might be suffering from leukemia. Give your reasons.
11. Most physicians would not diagnose leukemia on the basis of one test. What other conditions might explain the appearance of the test tube you chose in question 10? Give your reasons.
12. Lead poisoning can cause bone marrow destruction. Which of the subjects in **Figure 7** might have lead poisoning? Give your reasons.
13. Which subject in **Figure 7** lives at a high altitude? Give your reasons.

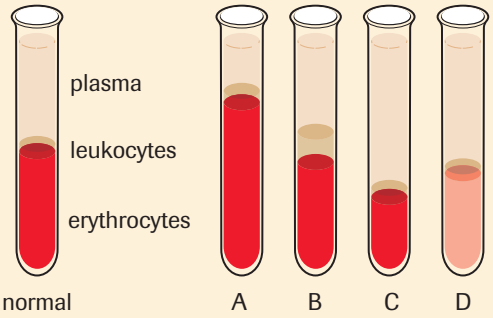


Figure 7

14. Athletes can take unfair advantage of the benefits of extra red blood cells. Two weeks prior to a competition, a blood sample is taken and centrifuged, and the red blood cell component is stored. A few days before the event, the red blood cells are injected into the athlete. Why would athletes remove red blood cells only to return them to their body later?
15. How does Rh+ blood differ from Rh– blood?
16. Explain why type O blood is considered the universal donor. Why is type AB the universal recipient?
17. What would happen if blood type A was transfused into people with blood types A, B, O, and AB? Provide an explanation for each case.
18. Why does a fetus with erythroblastosis fetalis develop anemia?

The Body's Lines of Defence 11.2

The human body must constantly defend itself against the many unwelcome intruders it encounters in the air, in food, and in water. It must also deal with abnormal body cells that sometimes turn into cancer. Three lines of defence have evolved to help resist infection and possible death from fatal illnesses. The first two lines of defence are considered nonspecific immune responses, meaning that they do not distinguish one microbe from another. The third line of defence—the immune system—is a specific immune response that reacts in specialized ways to various invaders. All the cells involved in the immune system develop from the bone marrow. (These cells were illustrated in **Figure 2**, Section 11.1, on page 350.)

The First Line of Defence

The body's first line of defence against foreign invaders is largely physical. Like a medieval city that used walls and moats to defend against attack from outsiders, the skin and mucous membranes defend against viral and bacterial invaders. Intact skin provides a protective barrier that cannot normally be penetrated by bacteria or viruses. The skin also has chemical defences in the form of acidic secretions, which keep it within a pH range of 3 to 5, acidic enough to inhibit the growth of microbes. Lysozyme, an antimicrobial enzyme secreted in human tears, saliva, mucous secretions, and perspiration, destroys the cell walls of bacteria, killing them.

In the respiratory tract, invading microbes and foreign debris become trapped in a layer of mucus and are filtered by tiny hairlike structures called cilia (**Figure 1**). The cilia move in waves, sweeping particles up toward the throat where coughing can expel them. Corrosive acids in the stomach and protein-digesting enzymes destroy most of the invading microbes carried into the body with food.

The Second Line of Defence

A second line of defence can be mobilized if the invader takes up residence within the body. Leukocytes, or white blood cells, may engulf invading microbes or produce antibodies.

The body's nonspecific defence mechanisms rely mainly on the process of **phagocytosis**, the ingestion of invading microbes by certain types of white blood cells. When a foreign particle penetrates the skin through an injury, special leukocytes, known as *monocytes*, migrate from the blood into the tissues, where they develop into **macrophages** (meaning "big eaters"). The macrophages extend long protrusions, called *pseudopods*, that attach to the surface of the invading microbe; the microbe is then engulfed and destroyed by enzymes within the macrophage.

In another phagocytic response, white blood cells called *neutrophils* are attracted to chemical signals given off by cells that have been damaged by microbes. In a process called *chemotaxis*, the neutrophils squeeze out of capillaries and migrate toward the infected tissue. The neutrophils then engulf the microbe and release lysosomal enzymes that digest both the microbe and the leukocyte. The remaining fragments of protein, dead white blood cells, and the digested invader are called **pus**. Tissue damage due to physical injury also initiates a localized **inflammatory response**—a nonspecific immune response resulting in swelling, redness, heat, and pain (**Figure 2**, next page). Pus and accompanying inflammation are sure signs that the second line of defence has been at work.

DID YOU KNOW ?

The Skin Is the Largest Organ

The skin is the largest organ of the body, accounting for as much as 15 % of the body's total mass. An area no larger than a dime will contain approximately 10 hairs, 15 oil glands, 3 blood vessels, 100 sweat glands, and 200 neurons.

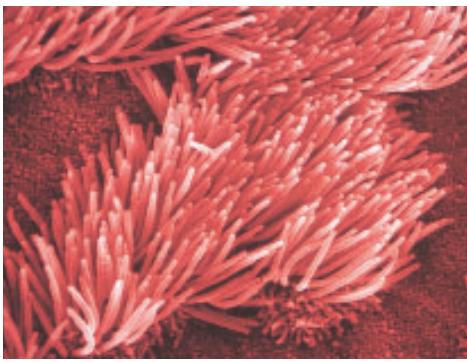


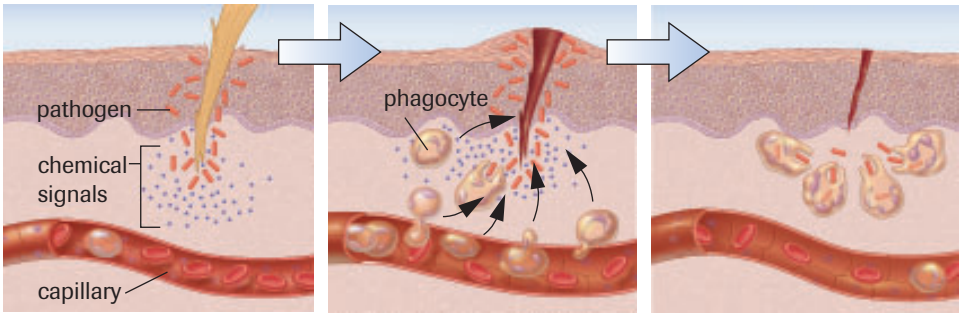
Figure 1
Cilia in the respiratory tract

phagocytosis the process by which a white blood cell engulfs and chemically destroys a microbe

macrophage a phagocytic white blood cells found in lymph nodes, bone marrow, and the spleen and liver

pus a thick liquid composed of protein fragments from digested leukocytes and microbes

inflammatory response localized nonspecific response triggered when tissue cells are injured by bacteria or physical injury, characterized by swelling, heat, redness, and pain



(a) At the first sign of injury, chemical signals are released by the foreign invader. Other chemicals—histamines and prostaglandins—are released by the cells of the body.

(b) Chemical signals cause the capillaries to dilate. Blood flow increases and the capillaries become more permeable. Other chemicals attract phagocytic cells and specialized white blood cells.

(c) Phagocytes engulf and digest the invaders and cellular debris, which promotes healing of the tissues.

Figure 2
Damage to tissue cells by bacteria or physical injury initiates a localized inflammatory response.

The body's nonspecific defence system responds to localized injuries, like a cut or puncture, but it can also respond with a system-wide defence to more severe damage or infection. Injured cells emit chemicals that stimulate the production of phagocytic white blood cells and increase their release into the bloodstream.

A fever is an example of the body's system-wide response to infection. When infectious organisms spread throughout your body, such as when you have a cold or flu, neutrophils and macrophages digest the invaders and release chemicals into your bloodstream. When these chemicals reach your hypothalamus, they reset the body's thermostat to a higher temperature—about 40 °C. A fever makes it difficult for harmful bacteria to survive; thus, the fever helps to prevent the proliferation of the infectious organisms. Reducing your fever by taking aspirin may actually prolong the infection. However, if your body temperature rises above 40 °C, it can be unsafe. For example, a fever of 41 °C may cause convulsions, especially in young children. Human cells cannot survive above 43 °C because proteins start to denature.

mini Investigation — Observing Phagocytosis

Protist models can be used to observe phagocytosis, the process by which macrophages engulf invaders (**Figure 3**).

Materials: prepared slide of amoeba, light microscope, medicine dropper, slide, cover slip, live amoeba culture, live yeast culture

- Obtain a prepared slide of amoeba that shows phagocytosis, and use a light microscope to look at it under high-power magnification.

(a) Draw what you see. Label the extension of false feet as "pseudopods" and indicate the food vacuole (if present).

- Using a medicine dropper, make a wet mount from a live amoeba culture. Observe the movement of the amoeba.
- Remove the cover slip from the slide and use a medicine dropper to add a drop of live yeast culture. Replace the cover slip and observe for phagocytosis.

(b) Describe the movement of the amoeba.
(c) Describe the process of phagocytosis.

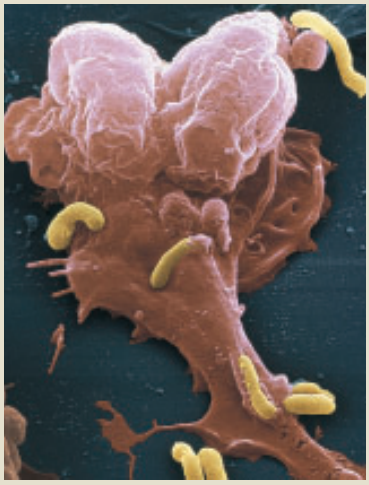


Figure 3
The macrophage has long, sticky extensions of cytoplasm that draw bacteria toward the macrophage. Once the bacteria come in contact with the macrophage, they are engulfed and destroyed.

The Immune Response (The Third Line of Defence)

Although some macrophages migrate throughout the body, others reside permanently in body tissues, such as the brain, lungs, kidneys, liver, and connective tissues. The fixed macrophages that reside in the spleen, lymph nodes, and other tissues of the lymphatic system trap and filter out microorganisms and foreign invaders that enter the blood. (Refer to **Figure 3**, Section 10.4, on page 338, for an illustration of the lymphatic system.)

The appearance of foreign organisms in the body activates antimicrobial plasma proteins, called **complement proteins**. There are about 20 known types of complement proteins. Under normal conditions, these proteins are present in the circulatory system in an inactive form. Marker proteins from invading microbes activate the complement proteins, which, in turn, serve as messengers. The proteins aggregate to initiate an attack on the cell membranes of fungal or bacterial cells. Some of the activated proteins trigger the formation of a protective coating around the invader, as shown in **Figure 4 (a)**. This coating seals the invading cell, immobilizing it. A second group punctures the cell membrane, as seen in **Figure 4 (b)**. Water enters the cell through the pore created by the protein, causing the cell to swell and burst. A third group of proteins attaches to the invader, as illustrated in **Figure 4 (c)**, making it more susceptible to phagocytosis by leukocytes.

complement protein a plasma protein that helps defend against invading microbes by tagging the microbe for phagocytosis, puncturing cell membranes, or triggering the formation of a mucous coating

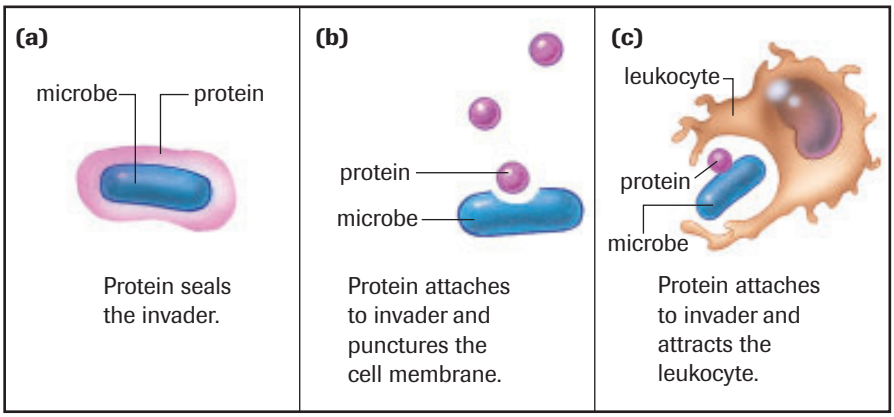


Figure 4
Complement proteins aid the immune response.

Also involved in the immune response are lymphocytes, a type of white blood cell that produces antibodies. An antibody is a protein molecule that protects the body from invaders. All cells have special markers located on their cell membranes. Normally, the immune system does not react to the body's own markers. However, intruding cells or foreign proteins activate the production of antibodies. The cell membrane of a bacterium and the outer coat of a virus contain many different antigens. The antigen (a term derived from antibody generator) may even be a toxin produced by moulds, bacteria, or algae. The toxin presents a danger to the cells of the body because it interferes with normal cell metabolism.

Two different types of lymphocytes are found in the immune system. The first is the **T cell**, which is produced in the bone marrow and stored in the thymus gland, from which the T cell receives its name. The T cell's mission is to seek out the intruder and signal the attack. Acting much like a sentry, one type of T cell identifies the invader by its antigen markers (**Figure 5**), which are located on the cell membrane. Once the antigen is identified, another T cell passes this information on to the antibody-producing **B cell**.

T cell a lymphocyte, manufactured in the bone marrow and processed by the thymus gland, that identifies and attacks foreign substances

B cell a lymphocyte, made and processed in the bone marrow, that produces antibodies

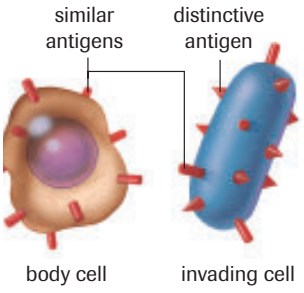


Figure 5
Sugar-protein complexes located on the cell membrane act as markers. T cells distinguish the markers on the body's cells from those of invading cells.

EXTENSION

Producing Monoclonal Antibodies

Have you ever wondered where synthetic antibodies come from? This Audio Clip provides a step-by-step description of the synthetic process used by industry to produce large quantities of identical antibodies.

www.science.nelson.com GO

B cells multiply and produce molecular weapons: the antibodies. Each B cell produces a single type of antibody, which is displayed along its cell membrane. Eventually, the B cells are released from the bone marrow and enter the circulatory system. Some B cells differentiate into super-antibody-producing cells called *plasma cells*. These plasma cells can produce as many as 2000 antibody molecules every second.

Antigen–Antibody Reactions

Antibodies are Y-shaped proteins engineered to target foreign invaders. Antibodies are specific; this means that an antibody produced against the influenza virus, for example, is not effective against HIV, the virus that causes acquired immunodeficiency syndrome (AIDS). The tails of these Y-shaped proteins are very similar regardless of the type of antibody. Variations exist only at the outer edge of each arm, the area in which the antibody combines with the antigen (**Figure 6**). Antigen markers found on the influenza virus are different from those found on HIV. Each antibody has a shape that is complementary to its specific antigen. Thus, the binding site of an antibody produced in response to the influenza virus will not complement HIV.

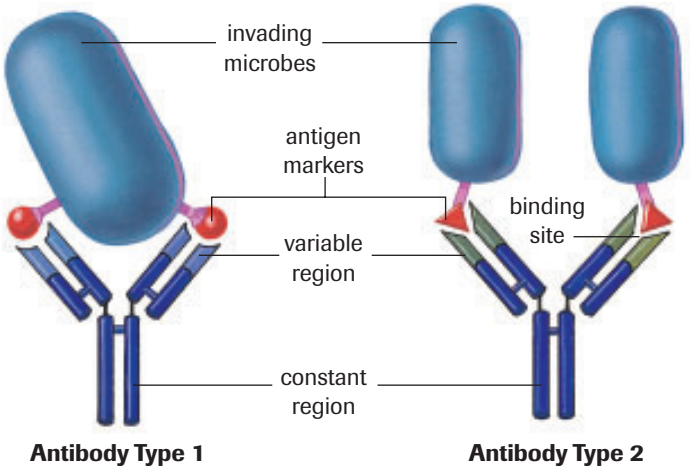


Figure 6
Each type of antibody will combine only with the appropriate antigen.

receptor site a port along a cell membrane into which hormones, nutrients, and other needed materials fit

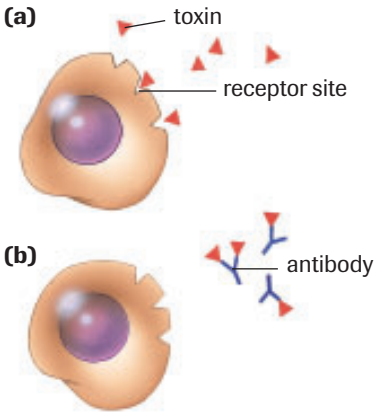


Figure 7
(a) Toxin binds to receptor.
(b) Antibody binds to toxin.

Many different antigen markers are located on the membrane of a virus or bacterium. Although different antibodies can attach to the invader, each antibody attaches only to its complementary marker. The attachment of antibodies to the antigens creates an antigen–antibody complex, which is larger and more conspicuous and, therefore, more easily engulfed and destroyed by the circulating macrophages.

How do antibodies prevent poisons, or toxins, from destroying cells? Specialized **receptor sites** are found on different cells, which may explain why some poisons affect the nervous system while others affect the digestive or circulatory system. The receptor site is designed to accommodate either a hormone or a specific nutrient. Unfortunately, the toxin has a shape similar to a hormone or nutrient that allows it to become attached to the receptor sites on cell membranes. Once attached, the poison is engulfed by the cell, which assumes that it is actually a needed substance. Antibodies interfere with the attachment of toxins to the cell membranes' receptor sites by binding to the toxins, as shown in **Figure 7**.

Viruses also use receptor sites as entry ports. The virus injects its hereditary material into the cell, but most often leaves the outer protein coat in the receptor site. Because of this outer coat, different viruses attach to different types of cells. For example, the outer

coat of the cold virus has a geometry that enables it to attach to lung cells. HIV attaches to the receptor sites of the T cell (**Figure 8**). Once attached, the virus is engulfed by a T cell, creating another problem for the immune system. Antibody production requires a blueprint of the invader, but the protein coat of the virus hides inside the very cells assigned as sentries for invading antigens. Does this provide a clue as to why the body experiences difficulty defeating HIV?

Antibodies attach themselves to invading viruses, thereby preventing the viruses from binding to receptor sites on cells. For some viruses, the antibody will cause the virus to change shape, so it cannot bind to a cell. Occasionally, the outer coat of an invader will change shape slightly because of mutations. The mutated viruses can still gain access to a receptor site but are not tied up by an antibody.

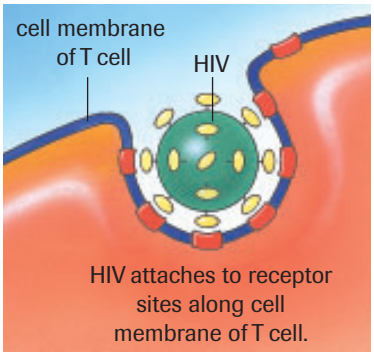


Figure 8
HIV has a shape that provides access to the T cell. The T cell engulfs HIV, unlike most other viruses.

Case Study

Bovine Spongiform Encephalopathy

Bovine spongiform encephalopathy (BSE) belongs to a larger group of transmissible spongiform encephalopathy (TSE) diseases that are characterized by the spongy deterioration of the brain. Transmissible means that the disease can pass from one animal to another. Eventually, BSE destroys the nervous system and causes death.

Spongiform encephalopathy is found in animals other than cattle. Scrapie affects sheep and goats. Chronic wasting disease (CWD) affects mule deer, white-tailed deer, and elk. Creutzfeldt-Jakob Disease (CJD) is a rare and fatal form of TSE that affects humans. Variant Creutzfeldt-Jakob disease (vCJD) has been diagnosed since 1996 and is thought to be linked to the consumption of meat products derived from BSE cattle.

What Causes the Disease?

The most widely accepted theory is that an agent, called a prion (**Figure 9**), infects the host and causes the conversion of normal proteins into abnormal proteins, which accumulate in the brain tissue and change its structure to a spongy form.

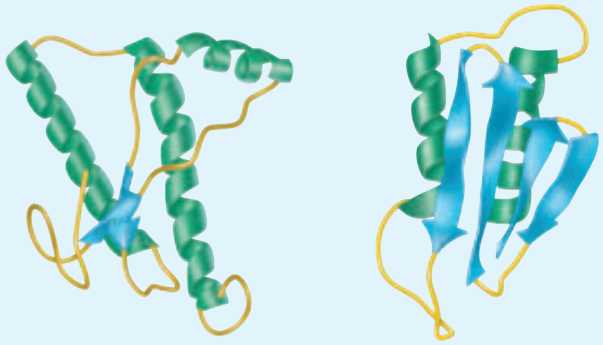


Figure 9
A normal prion (left) compared to the infectious form (right) that causes BSE. The structures of the proteins are shown using the ribbon model for ease of comparison.

Prions have caused the scientific community to examine disease in a new manner. Prions are proteins that are self-replicating, but, unlike other disease-causing agents, prions do not contain genetic material. Most prions are highly resistant to heat, freezing, and chemical sterilization.

The Origin of the Disease

Different and sometimes competing theories about the origin of this disease propose the possibility that BSE occurred at undetectable levels long before it was identified in British cattle in 1986. Many experts believe that BSE may have been caused by feeding ruminant (cattle, sheep, goats, deer, elk, bison) protein products to cattle. The prion could have been introduced to cattle from infected feed. One theory suggests that the protein may have come from another TSE, such as scrapie. Scrapie in sheep has been in existence for hundreds of years. When the protein from the sheep changed shape, it may have jumped species to the cow.

The recycling of proteins such as brain tissue and bone within cattle feed seems to be the problem. This practice dates back at least to the 1920s. It was originally seen as an inexpensive way to boost milk production and increase weight gain in cattle. The recycling of animal protein, known as rendering, is still regarded as an efficient way to utilize nutritious materials that would otherwise be wasted. Rendering serves the public interest by

- controlling the spread of pathogens that grow on waste tissues.
- reducing air pollution. Incinerating animal wastes as another means of disposal would reduce air quality.
- reducing wastes from packing plants. Approximately 50 % of every cow and about 30 % of every pig are not consumed by humans.

Understanding the Threat

Many scientists believe the disease began long before the first case of BSE was recorded in 1986 in England. A long incubation period (4 to 5 years) before the disease manifests itself indicates that it may have appeared in the 1970s.

In Canada, the first case of BSE was reported in 1993, in a beef cow imported from Britain in 1987. In 1997, feed-practice controls were put in place by the federal government of Canada. High-risk tissues such as cow brain and spinal cord could not be added to cattle feed. The second case was found in Alberta on May 20, 2003. The herd was immediately destroyed. Infected feed was identified as the most likely cause. The United States, along with other nations, closed the border to Canadian beef. In January 2005, two more Canadian cases of BSE were confirmed.

In March 1996, vCJD was diagnosed in people living in Britain and France. In August 2002, doctors confirmed that a Saskatchewan man died from vCJD, the human counterpart to BSE. The man was known to have spent time in Britain and may have acquired the disease there.

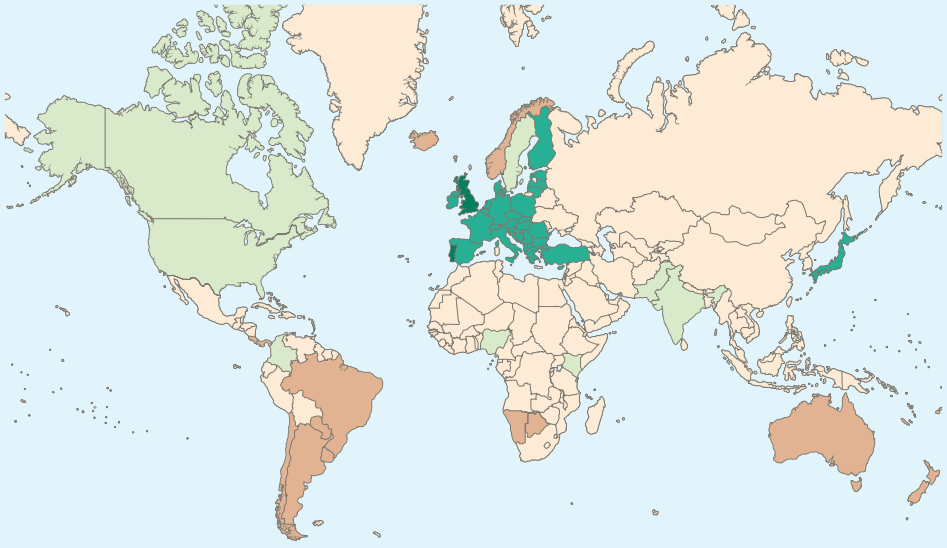
Evaluating Safety

- Canada had 13.5 million cows in 2005, with about 5.7 million (42 %) in Alberta.
- There had been four confirmed cases by January 2005, but one was from an imported cow. Only three cases were from cows native to Canada.
- To prevent prions from entering the food chain, rendering plants do not use sheep infected with scrapie, elk or deer infected with CWD, or high-risk cattle. Brain and spinal cord tissue are not used in feed.
- All ruminant products from countries that pose a risk of BSE are banned from Canada.
- All rendered proteins from cattle were banned from cattle feed in 1997.
- Feed practices are similar in the United States and Canada. Feed products are exported and imported between the two countries.
- BSE prions have never been found in dairy products.
- Random testing of beef cattle for BSE is routinely conducted. The testing frequency increased dramatically in 2003.

Case Study Questions

1. According to the map provided by the European Commission in 2002 (**Figure 10**), assess the risk presented for Canada.
2. According to the evidence presented, do cattle from Canada present higher levels of risk than those from the United States? Give your reasons.
3. According to the data provided, make a prediction about the country that might have been the original site of this disease. Give your reason.
4. Explain why it is difficult to provide a worldwide perspective on the spread of BSE.
5. How are prions unlike viruses and bacteria?
6. What would normally happen to a protein exposed to extreme heat?
7. Why would prion resistance to heat cause concern among humans?

Geographical BSE Risk



The geographical BSE risk (GBR) is a qualitative indicator of the likelihood of one or more cattle being infected with BSE, pre-clinically as well as clinically, at a given point in time.

no data: | Category 1: highly unlikely | Category 2: unlikely but not excluded | Category 3: likely but not confirmed or confirmed at a lower level | Category 4: confirmed, at a higher level

Source: European Commission, Scientific Steering Committee on the Geographical Risk of BSE (GBR), August 2002

Figure 10
BSE risk by country

8. Suggest a way of controlling the disease.
9. Explain why beef cattle under three years of age pose less threat.
10. Compare the BSE trends in and outside the UK using the graphs in **Figure 11**.
11. According to **Figure 11 (b)**, what was the worst year for BSE cases within the UK? What was the total number of cases?
12. Why would government officials want to know the age of infected cows?
13. Make two generalizations from the graph presented in **Figure 12**.
14. The decline in vCJD deaths from 2000 to 2001 (**Figure 12**) indicates fewer cases; however, it may not indicate that the disease is being eradicated. Why should caution be used in claiming that vCJD has been conquered?
15. Assess the risk of eating beef for humans.
16. What additional safety measures would you suggest?

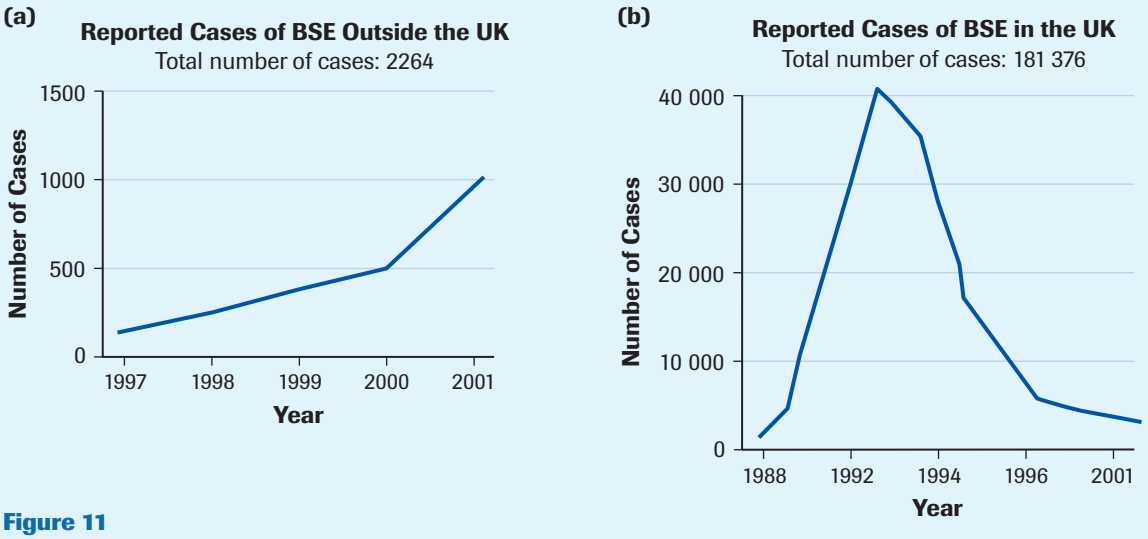


Figure 11
Reported cases of BSE

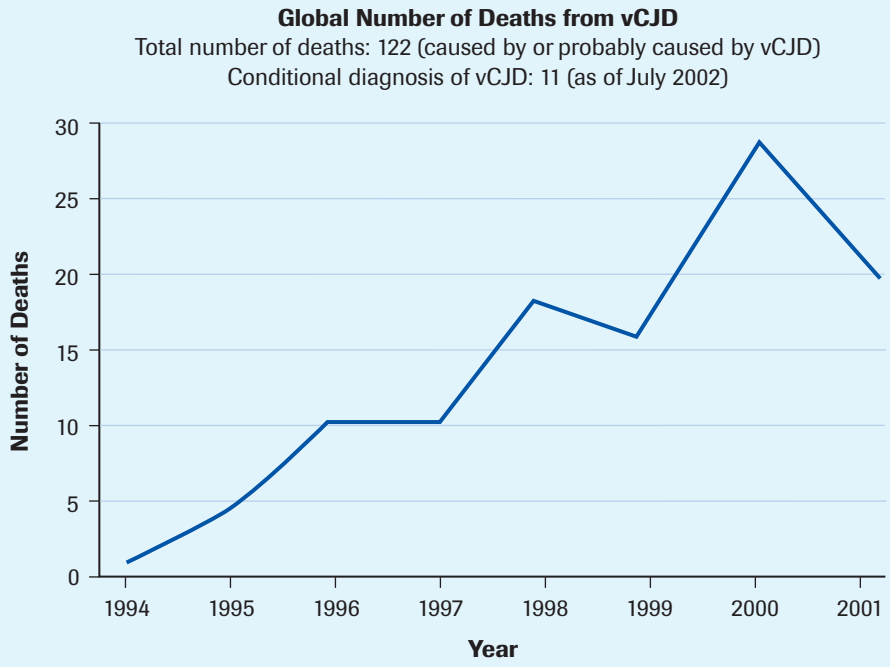


Figure 12
Global deaths from vCJD

Recognizing Harmful Antigens

Figure 13 illustrates how the body recognizes harmful antigens. The T cells roam the body in search of foreign invaders that pose a threat to survival. The macrophages attack the invaders and engulf them. The foreign antigen markers are not destroyed with the invader but are pushed to the cell membrane of the macrophage. Pressing the antigens into its cell membrane, the macrophage couples with T cells referred to as **helper T cells**. The T cells read the antigen's shape and release a chemical messenger called **lymphokine**. The lymphokine causes the B cells to divide into identical cells called clones. Later, a second message is sent from the helper T cells to the B cells, triggering the production of antibodies. Each B cell produces a specific type of antibody. By the time the B cells enter the circulatory system, many antibodies are attached to their cell membranes.

helper T cell a T cell with receptors that bind to fragments of antigens

lymphokine a protein produced by the T cells that acts as a chemical messenger between other T cells and B cells

killer T cell a T cell that destroys microbes, body cells infected with viruses, and mutated cells by puncturing cell membranes

The helper T cells activate an additional defender, the **killer T cells**. As the name suggests, these lymphocytes carry out search-and-destroy missions. Once activated, the killer T cells puncture the cell membrane of the intruder, which may be a fungus, protozoan parasite, or bacterium. Viruses, however, are much more insidious because they hide within the confines of the host cell. Here, the true value of the killer T cells is demonstrated. Once the viral coat is found attached to the cell's membrane, the T cell attacks the infected cell. By destroying the infected body cell, the killer T cell prevents the virus from reproducing.

EXTENSION

Four Pathways to Achieve Immunity

How do you gain immunity to different diseases? This Audio Clip will discuss the four different ways to acquire immunity to specific diseases.

www.science.nelson.com GO

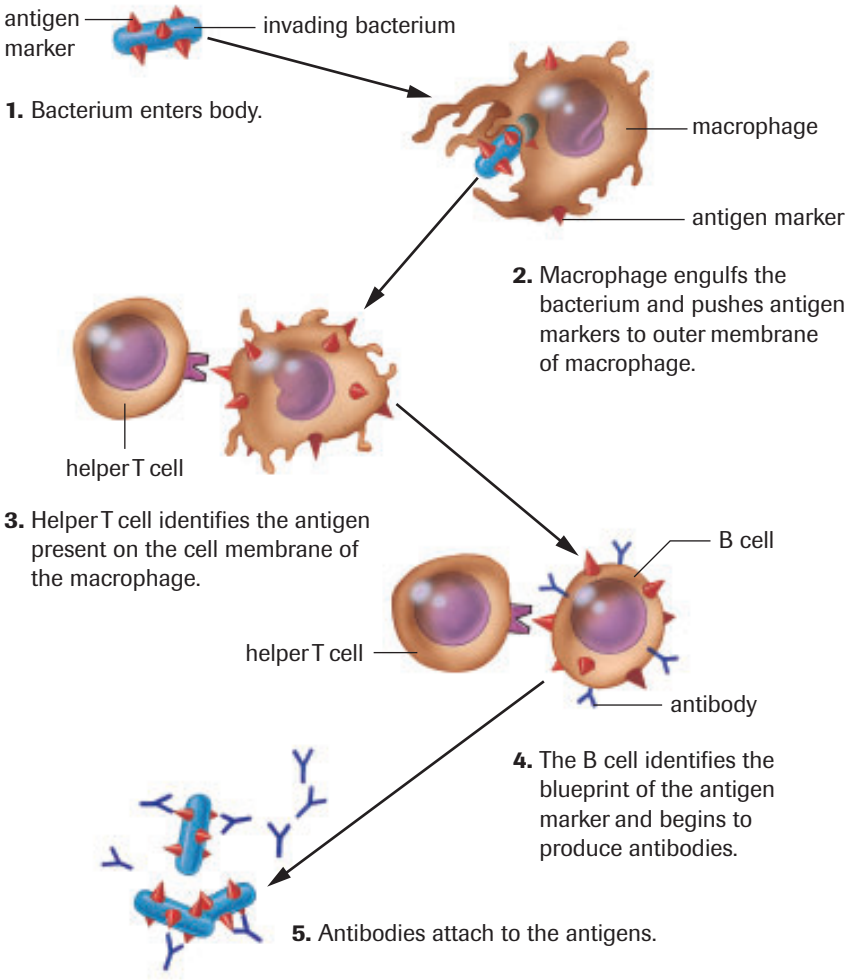


Figure 13
The immune system recognizes harmful antigens.

Killer T cells also destroy mutated cells (**Figure 14**). This is an extremely important process because some of the altered cells may be cancerous. Many experts believe that everyone develops cancerous cells, but, in most cases, the T cells eliminate them before a tumour forms. Killer T cells may also account for the body's rejection of transplanted organs. Antigen markers on the cell membranes of the donor will be different from those of the recipient. Once the foreign markers of the transplanted tissue are recognized, the recipient's killer T cells initiate an assault. Immunosuppressant drugs, such as cyclosporin, can slow the killer T cells. Unfortunately, individuals who receive these drugs become susceptible to bacterial infections. One of the leading causes of death for an organ transplant patient is pneumonia.

Once the battle against foreign invaders has been won, another T cell, the **suppressor T cell**, inhibits the immune system response. Communication between the helper T cells and the suppressor T cells ensures that the body maintains adequate numbers of antibodies to contain the invading antigen. Most of the B cells and T cells will die off within a few days after the battle, but a small contingent will remain long after to guard the site. Phagocytes survey the area, cleaning up the debris left from dead and injured cells.

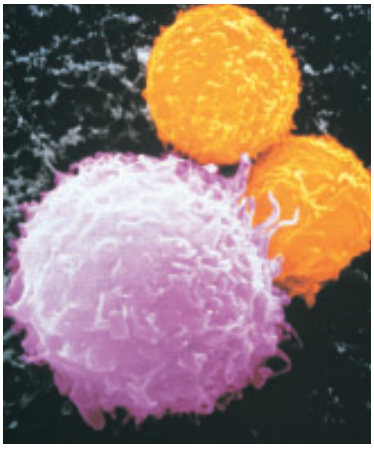


Figure 14
Killer T cells bind with a tumour cell.

suppressor T cell a T cell that turns off the immune system

The Immune System's Memory

The Aboriginal population of Hawaii was nearly annihilated by measles in the late 18th and early 19th centuries after British explorer James Cook and his sailors unwittingly introduced the disease when they arrived at the Hawaiian Islands. In North America, the Aboriginal population was decimated by epidemics of smallpox. Because neither group had been exposed to these viruses before, they had no antibodies to fight infection. At this time, Europeans and Asians, unlike the Aboriginal populations of Hawaii and North America, had long been exposed to many types of viruses and were better able to produce antibodies to fight them.

As mentioned earlier, the helper T cells must read a blueprint of the invader before B cells produce antibodies. This blueprint is stored even after the invader is destroyed so that subsequent infections can be stopped before the microbe gains a foothold. Immunity is based on maintaining an adequate number of antibodies. It is believed that a **memory B cell** is generated during the infection. Like helper T cells, the memory B cells hold an imprint of the antigen that characterizes the invader. Most T cells and B cells produced to fight the infection die within a few days; however, the memory B cells remain. During a subsequent infection, the memory B cells identify the invader and quickly mobilize antibody-producing B cells. Invading pathogens are defeated before they become established. As long as the memory B cell survives, the individual is immune.

EXTENSION

Immune Memory
Watch this brief simulation of how B cells help the body respond faster to antigens the body has encountered before.

www.science.nelson.com GO

memory B cell a B cell that retains information about the shape of an antigen

WWW WEB Activity

Simulation—Virtual Immunology Laboratory

How does your immune system respond to foreign invaders? How do antibodies know which antigen to attack? Can the formation of antibodies be used to diagnose disease? In this activity, you will use an ELISA (enzyme-linked immunosorbent assay) to detect either the antigen or antibody associated with a disease-causing agent. After you have finished the simulation, create a model to depict how the main components of the immune system function.

www.science.nelson.com GO

SUMMARY The Body's Lines of Defence

- Skin and mucous membranes provide physical barriers that prevent most infectious organisms from entering the body.
- Leukocytes (white blood cells), produced in the bone marrow, fight infection in a variety of ways. Phagocytosis of invading microbes is one of the main methods used by certain leukocytes to combat infection.
- Tissue damage due to physical injury initiates the inflammatory response, which is a nonspecific immune response resulting in swelling, redness, heat, and pain.
- Antibodies attach to foreign antigens, such as microbes and toxins. Each antibody is specific and can only bind its complementary antigen.

Table 1 Lymphocytes Involved in the Immune Response

Cell	Function
helper T cells	act as sentries to identify foreign invading substances
B cells	produce antibodies
killer T cells	puncture cell membranes of infected cells, thereby killing the cell
suppressor T cells	turn off the immune system
memory B cells	retain information about the shape of an antigen

Section 11.2 Questions

1. How does lysozyme protect the body against invading microbes?
2. Outline protective mechanisms provided by the respiratory tract.
3. How do monocytes protect against microbes?
4. Explain why swelling and pus at the site of an injury are signs that the immune system is functioning.
5. Define and contrast these terms: antigen, antibody; T cell lymphocytes, B cell lymphocytes; macrophages, lymphocytes.
6. Explain how B cell, helper T cell, and killer T cell lymphocytes provide immunity.
7. How do antibodies defeat antigens? Describe four contributions that antibodies make to the immune system.
8. How do memory B cells provide continuing immunity?
9. A patient displaying a high fever may be asked by the physician to have blood tests done. One of these tests would likely be a white blood cell count. Explain what an abnormal result might indicate.
10. A research group has begun testing on a potential cure for type 1 diabetes, an inherited disease caused by the destruction of the insulin-producing cells in the pancreas by one's own immune system. An immunosuppressant drug is administered twice daily to a test group of 150 people.
    (a) Why can the immunosuppressant drug prevent diabetes?
    (b) Researchers found that the drug wasn't effective once symptoms for diabetes were expressed in test subjects. What conclusions can you draw about this?
    (c) Explain why researchers are working on a test to identify antibodies that destroy insulin-producing cells.
    (d) List three important research questions that remain to be answered.

Malfunctions of the Immune System 11.3

Abnormal functioning of the immune system can cause two types of problems: immunodeficiency diseases and inappropriate attacks of the immune system against non-threatening agents. Immunodeficiency diseases may be caused by a foreign agent, such as HIV, which attacks T cells, or a hereditary condition, such as severe combined immunodeficiency (SCID). The gene mutation that causes SCID results in the inability to produce B cells and T cells. Cancer therapy or prolonged exposure to anti-inflammatory drugs, such as cortisol, can also reduce the effectiveness of the immune system.

Inappropriate or exaggerated immune responses can also create problems. A hypersensitivity to harmless agents (an allergy) or a response in which the immune system begins to attack normal cells in one's own body (an autoimmune disease) can destroy tissues and organs.

Allergies

Allergies occur when your immune system mistakes harmless antigens for harmful invaders. If you are allergic to peanuts, your immune system recognizes one of the proteins in the peanut as dangerous. Although the protein is quite safe, your body mobilizes the antibody strike force against it. Tissue swelling and mucus secretion and, sometimes, constricted air passages are part of the immune response. Dust, ragweed, strawberries, and leaf moulds do not pose any direct threat to life, but the immune response to these agents can sometimes be so severe that it becomes life threatening.

A severe allergic reaction is an anaphylactic reaction (**Figure 1**), which involves the respiratory and circulatory systems. It often is accompanied by swelling of different body parts, hives, and itching. When you ingest something, like food or medicine, to which you are allergic, cells that "believe" they are endangered release a chemical messenger, called *bradykinin*, which stimulates the release of another chemical, *histamine*. Histamine is produced by the circulating white blood cells known as basophils and by mast cells found in connective tissues. Histamine changes the cells of the capillaries, increasing

DID YOU KNOW ?

Peanut Allergy

Peanut allergy is the most common cause of food anaphylaxis (anaphylactic shock from foods). Ingesting minute amounts can lead to a rapid reaction resulting in death within minutes. Because a reaction may recur even after an initial epinephrine injection, the affected person must be immediately hospitalized. Traces of peanut from a knife, plate, countertop, or even from kissing someone who has eaten peanuts can trigger a reaction. For those who are sensitive to peanuts, avoiding peanut products is crucial but also difficult. In Canada, annual peanut butter consumption is estimated to be about 3 kg per person. Many processed foods contain the ingredient "hydrolyzed vegetable protein," which may contain peanut protein.

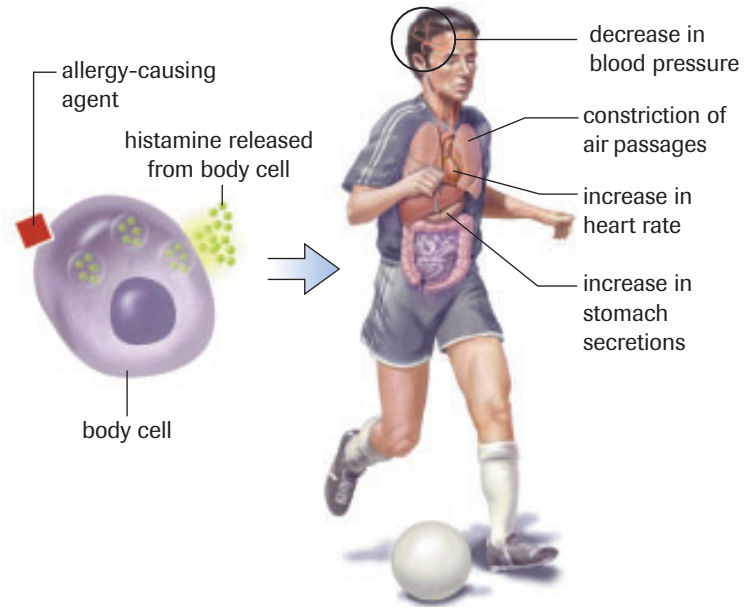


Figure 1
The body's response to an allergy-causing agent

permeability. The enlarged capillary causes the area to redden. Proteins and white blood cells leave the capillary in search of the foreign invader, but, in doing so, they alter the osmotic pressure. The proteins in the extracellular fluid create another osmotic force that opposes the osmotic force in the capillaries. Less water is absorbed into the capillaries, and tissues swell. These reactions can be brought on by drugs, vaccines, and some foods (peanuts, shellfish, eggs, berries, and milk) in individuals who are sensitive to these substances. Anaphylactic shock can occur very quickly. Weakness, sweating, and difficulty breathing are indicators of the condition. Nausea, diarrhea, and a drop in blood pressure may also occur. Medical precautions may range from carrying a kit with epinephrine to carrying antihistamines. People with severe food allergies should wear a medical alert bracelet or necklace and read all food labels carefully.

Autoimmune Diseases

The immune system can make mistakes. As you have already learned, allergies are caused when the immune system perceives harmless substances to be dangerous. The immune system can also go awry and launch an attack on the body's own cells. The renegade lymphocytes treat the body's cells as foreign and make antibodies to attach to their cell membranes. Many researchers believe that most people have mutated T cells and B cells that are capable of attacking the body; however, the renegade cells are usually held in check. The suppressor T cells play an important role in recognizing and intercepting the renegade T cells and B cells. One theory suggests that the suppressors secrete a substance that tells the macrophages to engulf the renegade cells.

The failure of the suppressor T cells to control the renegade cells can be seen in autoimmune diseases such as rheumatoid arthritis, in which an immune response is mounted against the connective tissues of the joints. Rheumatic fever, another autoimmune disorder, results from an exaggerated immune response that scars the heart muscle. Type 1 diabetes is caused by an immune reaction against the insulin-producing cells of the pancreas, and lupus is caused by the accumulation of antigen–antibody complexes that build up in the walls of blood vessels, joints, kidneys, and skin. Multiple sclerosis (MS) is an autoimmune disease in which T cells of the body initiate an attack on the myelin sheath of nerve cells. In the advanced stages of MS, paralysis results from the destruction of the insulation of the nerve cell provided by the myelin sheath.

Drugs or serious infections can weaken the suppressor T cells, leaving the body vulnerable to autoimmune diseases. We know that the number of suppressor T cells declines with age, increasing the incidence of rheumatoid arthritis and other autoimmune diseases. Some individuals are born with defective suppressor T cells. Although no single cure exists, immune-suppressing drugs have been developed that reduce the intensity of the attack by the renegade cells.

Organ Transplant Rejection

The main challenge with any tissue or organ transplant is the immune response of the recipient—that is, the immune system's ability to distinguish between "self" and "non-self." The donor organ is often identified as a foreign invader by distinctive protein markers on its cell membranes. The distinctive marker (known as major histocompatability complex, or MHC) is a protein fingerprint unique to each individual. The recipient makes antibodies designed to destroy the foreign invader.

Kidney transplants can be used as an example. Living donor kidneys account for about 15 % of all kidney transplants. Because humans are born with two kidneys, the donor is able to give one kidney without significant effects on quality of life. A single kidney can carry out the filtering and osmoregulatory functions of the body. To reduce rejections,

CAREER CONNECTION

Pathologist

Pathologists are medical doctors who diagnose diseases and advise other physicians and surgeons about the treatment of diseases such as cancer. Pathologists perform tests on human tissue and blood to determine the type and extent of disease. Forensic pathologists specialize in determining the cause of death in forensic investigations. Find out if this is a career direction for you.

www.science.nelson.com GO

DID YOU KNOW ?

Organ Donation in Canada

Canada's organ donation rate is among the lowest of all the developed countries—more than 3000 Canadians are waiting for an organ transplant. One organ donor can donate numerous organs and tissues including lungs, heart, liver, kidneys, pancreas, bowel, eye tissue, skin, heart valves, bone, tendons, veins, and ligaments. You can indicate your wish to become an organ donor on your health card. Discuss this decision with your family so your wishes are known.

attempts are made to match the MHC of the tissues of donors and recipients as closely as possible. For living donor transplants, physicians usually look to close relatives because the MHC is genetically controlled. The better the match, the greater the chances of long-term success.

Kidney transplants from recently deceased donors account for the vast majority of transplants. However, the need for organs far surpasses supply (**Figure 2**). Again, as with living donors, close matching is essential. Not every donor kidney is appropriate for a specific recipient. To help reduce rejection, even for close matches, immunosuppressant drugs can be given. However, a drug that minimizes the fight against foreign tissues will also reduce the immune system's ability to fight off invading viruses and bacteria. These drugs place patients at risk of infections.

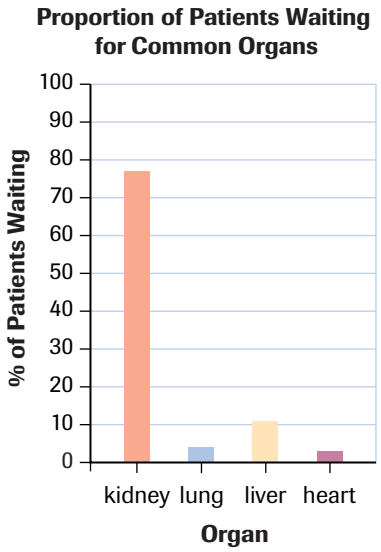


Figure 2
Percentage of all patients waiting for a transplant, by organ type. Kidney transplants are the second most common transplant in Canada (corneal transplants rank number one) and the most common organ transplant.

Organ Transplants in Alberta

Alberta's Capital Health Regional Transplant Program, located at the University of Alberta Hospital and Stollery Children's Hospital in Edmonton, provides transplants for adults and children from Alberta, Saskatchewan, the Northwest Territories, and British Columbia (**Table 1**). Its survival rates are among the best in Canada, and it is the only program in the country that provides all types of organ and tissue transplants.

The HOPE (Human Organ Procurement and Exchange) Program is responsible for the coordination, recovery, and distribution of organs in Alberta. HOPE also promotes awareness of organ and tissue donation. The Comprehensive Tissue Centre is one of only two accredited tissue banks in Canada. Transplanted tissues include eyes (cornea and sclera), skin, heart valves, and bone.

Stem Cell Research

The answer for replacing damaged tissues and organs may lie in stem cell research rather than transplantation. Stem cells can develop into a variety of different tissues such as epithelial, muscle, or nerve. Intestinal stem cells reline the gut; skin stem cells replace cells that are continuously sloughed off; and stem cells in the bone marrow give rise to a wide range of blood cells. Stem cells are **pluripotent cells**, meaning they can give rise to different types of body cells.

In 1998, James Thomson, a researcher at the University of Wisconsin, demonstrated that human stem cells could transform into a variety of cells, such as those that form the bone marrow, brain, muscle, skin, pancreas, liver, or practically any human tissue. If it were possible to regulate the development of human stem cells, the cells could replace destroyed islet cells that produce insulin, repair damaged cartilage, or repair cardiac tissue that has been destroyed by heart disease.

Dr. Freda Miller and colleagues at the Montreal Neurological Institute (MNI) have discovered multipotent stem cells in adult skin. These skin cells can be directed to become neurons or even muscle cells.

Table 1 Alberta's Capital Health Regional Transplant Program, 2004

Organ transplanted	Quantity
heart	28
heart/lung	1
lung	24
liver	71
kidney	84
kidney/pancreas	13
pancreas	1

pluripotent cell a cell that is capable of developing into a number of specialized cell, such as neuron or muscle cell

EXPLORE an issue

The Future of Stem Cell Research

The greatest challenge of organ transplants is to trick the recipient's immune system into accepting the new organ. Finding someone with a close tissue match to donate an organ can be extremely difficult. What if the person who needs a transplant could use his or her own stem cells to repair the damaged organ?

Statement

Governments should redirect some funding from organ transplant research to autologous (i.e., originating from the same individual) stem cell research.

1. Investigate this rapidly changing field of research. Search for information in newspapers, periodicals, CD-ROMs, and on the Internet.

www.science.nelson.com GO

Issue Checklist

○ Issue	○ Design	● Analysis
● Resolution	● Evidence	● Evaluation

2. Prepare a list of points and counterpoints. You might consider these questions:
   (i) Researchers are working on ways to use mature cells as a source for stem cells. How will this change the prospects for successful treatment?
   (ii) Companies have applied for patents on specific stem cells and techniques used to culture stem cells. These companies will own a medical procedure and collect huge royalties. Should this be allowed?
   (iii) Speculate why many people object to stem cell research.
   (iv) Why are governments regulating this field of research?
3. Decide whether you agree or disagree with the statement.
   (a) Prepare an outline.
   (b) Write your position paper.
   (c) Prepare to defend your position in class.

SUMMARY Malfunctions of the Immune System

- Abnormal functioning of the immune system can cause two types of problems: immunodeficiency diseases and inappropriate immune responses (allergic reactions and autoimmune diseases).
- Allergies occur when the immune system mistakes harmless antigens for harmful invaders.
- Autoimmune diseases occur when lymphocytes treat the body's cells as foreign.

Section 11.3 Questions

1. What are allergies?
2. Explain how an allergic reaction to peanuts can be life threatening.
3. Why is epinephrine administered as a treatment for a severe allergic reaction?
4. What causes autoimmune diseases?
5. What evidence suggests that suppressor T cells may be a significant factor in autoimmune diseases?
6. Why do donor organs have to be matched to the recipients?
7. Select an autoimmune disease and research the latest medical advance toward a cure. Search for information in newspapers, periodicals, CD-ROMs, and on the Internet.

www.science.nelson.com GO

8. Research the role of histamines in an allergic reaction.

INVESTIGATION 11.1

Diagnosing Disease by Examining Blood Cells

Report Checklist

- Purpose
- Problem
- Hypothesis
- Prediction
- Design
- Materials
- Procedure
- Evidence
- Analysis
- Evaluation
- Synthesis

White blood cell counts can be used as clues in the diagnosis of disease. In this activity, you will examine prepared slides to identify different types of white blood cells and to determine how changes in blood cell counts are used to diagnose disease.

The slides have been prepared using Wright's stain, which allows you to clearly view cells and many types of microorganisms. Wright's and similar stains for blood and bone marrow smears are mixtures of acidic and basic dyes. According to the number of acid and basic groups present, cell components absorb the dyes from the mixture in various proportions.

Materials

prepared slide of human blood
light microscope
lens paper

Procedure

1. Before beginning the investigation, clean all microscope lenses with lens paper and rotate the nosepiece to the low-power objective. Place the slide of blood on the stage, and focus under low power. Locate an area in which individual blood cells can be seen.
2. Rotate the revolving nosepiece to the medium-power objective and focus. Red blood cells greatly outnumber white blood cells.

(a) Draw a single human red blood cell.

(b) Estimate the size of the human red blood cell. Show your calculation.

3. Scan the field of view for different white blood cells. Using the classification of leukocytes provided in **Table 1**, classify the leukocytes and record your results.
4. Repeat the procedure by scanning 10 different visual fields. Record the data in your table.

Analysis

(c) Explain why few blood tests provide a diagnosis of disease.

Table 1 Classification of Leukocytes

Type	Description	Normal proportion (%)	Observed number	Observed proportion (%)
Granulocyte	granular cytoplasm			
neutrophil	3-lobed nucleus, 10 µm (Wright's stain: purple nucleus, pink granules)	65		
eosinophil	2-lobed nucleus, 13 µm (Wright's stain: blue nucleus, red granules)	2–4		
basophil	2-lobed nucleus, 14 µm (Wright's stain: blue–black nucleus, blue–black granules)	0.5		
Agranulocyte	nongranular cytoplasm			
monocyte	U-shaped nucleus, 15 µm (Wright's stain: light bluish–purple nucleus, no granules)	4–7		
lymphocyte (small)	large nucleus, 7 µm (Wright's stain: dark bluish–purple nucleus, no granules)	2–3		
lymphocyte (large)	large nucleus, 10 µm (Wright's stain: dark bluish–purple nucleus, no granules)	20–25		

INVESTIGATION 11.1 *continued*

Synthesis

Blood tests are used to help diagnose disease. **Table 2** shows some changes in leukocyte counts and the conditions associated with those changes. Use **Table 2** to answer the following questions:

(d) Why would a physician not diagnose leukemia based on a single blood test?

(e) What information might a blood test provide about a patient being treated for the lung disease tuberculosis? Why would blood tests be taken even after the disease has been diagnosed?

(f) Leukemia can be caused by the uncontrolled division of cells from two different sites: the bone marrow or lymph nodes. Indicate how blood tests could be used to determine which site harbours the cancerous tumour.

(g) Do blood donors need to have their blood counts taken? Why or why not?

Table 2 Health Conditions Associated with Abnormal Leukocytes

Leukocyte change	Associated conditions
increased eosinophils	allergic condition, cholera, scarlet fever, granulocytic leukemia
increased neutrophils	toxic chemical, newborn acidosis, hemorrhage, rheumatic fever, severe burns, acidosis
decreased neutrophils	pernicious anemia, protozoan infection, malnutrition, aplastic anemia
increased monocytes	tuberculosis (active), monocytic leukemia, protozoan infection, mononucleosis
increased lymphocytes	tuberculosis (healing), lymphocytic leukemia, mumps

Chapter 11 SUMMARY

Outcomes

Knowledge

- describe the main components of blood and their role in transport, blood clotting, and in resisting the influence of pathogens, i.e., erythrocytes, leukocytes, platelets, plasma (11.1, 11.2)
- describe the ABO and Rh blood groups on the basis of antigens and antibodies (11.1)
- explain the sequence of the blood clotting process (11.1)
- describe and explain, in general terms, the function of the lymphatic system (11.2)
- list the main cellular and non-cellular components of the human defence system and describe their role, i.e., skin, macrophage, helper T cell, B cell, killer T cell, suppressor T cell, and memory B cell (11.2)

STS

- explain how Canadian society supports scientific research and technological development that help achieve a sustainable society, economy, and environment (11.2)
- explain that decisions regarding the application of scientific and technological developments involve a variety of perspectives (11.3)

Skills

- conduct investigations and gather and record data and information by: determining the morphology and abundance of cellular components in a prepared human blood slide (11.1) and; researching and designing a simulation or model of the functioning of the main components of the human immune system (11.2)
- analyze data and apply mathematical and conceptual models (11.2)
- work as members of a team and apply the skills and conventions of science (all)

Key Terms

11.1

plasma
erythrocyte
anemia
leukocyte
platelet
thrombus
embolus
antigen
antibody
agglutination

11.2

phagocytosis
macrophage
pus
inflammatory response
complement protein
T cell
B cell
receptor sites
helper T cell
lymphokine
killer T cell
suppressor T cell
memory B cell

11.3

pluripotent cell

MAKE a summary

1. Imagine a microbe entering your blood. Create a flow chart or diagram that shows how the immune system would respond to this potentially dangerous situation. Label the diagram with as many of the key terms as possible.
2. Revisit your answers to the Starting Points questions at the start of the chapter. Would you answer the questions differently now? Why?

Go To www.science.nelson.com GO

The following components are available on the Nelson Web site. Follow the links for *Nelson Biology Alberta 20–30*.

- an interactive Self Quiz for Chapter 11
- additional Diploma Exam-style Review Questions
- Illustrated Glossary
- additional IB-related material

There is more information on the Web site wherever you see the Go icon in the chapter.

EXTENSION

CBC radioONE QUIRKS & QUARKS

The Path of Least Resistance: Alternatives to Antibiotics

More and more strains of bacteria are appearing that are resistant to antibiotics. Three researchers, Dr. Tania Watts (University of Toronto), Dr. Bob Hancock (University of British Columbia), and Dr. Gregor Reid (University of Western Ontario), discuss their research into alternatives to antibiotics.

www.science.nelson.com GO

EXTENSION

Pandemic Flu

This *NOVA* video investigates the question: Will the virus that causes bird flu develop the ability to move from person to person?

www.science.nelson.com GO

Chapter 11 REVIEW

Many of these questions are in the style of the Diploma Exam. You will find guidance for writing Diploma Exams in Appendix A5. Science Directing Words used in Diploma Exams are in bold type. Exam study tips and test-taking suggestions are on the Nelson Web site.

www.science.nelson.com GO

DO NOT WRITE IN THIS TEXTBOOK.

Part 1

1. The introduction of a microbe into the bloodstream will result in the production of (1) _____ by (2) _____.
   A. (1) antigens, (2) erythrocytes
   B. (1) antibodies, (2) erythrocytes
   C. (1) antigens, (2) leukocytes
   D. (1) antibodies, (2) leukocytes

2. Identify two functions of proteins found in the plasma.
   A. acting as antigens and blood clotting
   B. acting as antibodies and maintaining osmotic balance
   C. carrying oxygen and clotting blood
   D. phagocytosis and acting as antibodies

3. The ability of blood to clot can be reduced by
   A. ruptured platelets
   B. low calcium concentration in the blood
   C. high levels of thrombin
   D. high levels of iron in red blood cells

4. Identify which of the following is not involved in the body's defence system.
   A. skin
   B. erythrocytes
   C. macrophages
   D. cilia

Use the following information to answer questions 5 and 6.

A kinesiologist measured the factors related to circulation shown in **Table 1** in four different subjects.

Table 1 Cardiovascular Measurements of Four Subjects

Measurement	Subject W (normal)	Subject X	Subject Y	Subject Z
cardiac output (L/min)	5.1	7.2	5.4	4.0
white blood cell count (per mm^3 of blood)	8000	7900	15 000	8200
O_2 content of arterial blood (mL/100 mL of blood)	19.5	10.2	19.0	17.5

5. Which subject is most likely suffering from a bacterial infection?
   A. Subject X: low levels of oxygen in the blood occur when someone has an infection
   B. Subject Y: higher leukocyte levels produce more antibodies
   C. Subject Z: lower cardiac output conserves energy
   D. Subject Y or Subject Z: both have higher cardiac output to deliver more nutrients to tissues

6. Which subject is most likely suffering from anemia?
   A. Subject X: low levels of oxygen occur in the blood when someone has an infection
   B. Subject X: low levels of oxygen occur with a deficiency of hemoglobin
   C. Subject Y: higher leukocyte levels produce more antibodies
   D. Subject Z: low cardiac output conserves energy

Use the information in **Figure 1** to answer questions 7 and 8.

Antigens and Antibodies of Four Blood Groups

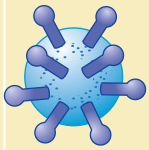
Group	1	2	3	4
antigens on red blood cells	A antigen 	B antigen 	A and B antigens 	no A or B antigens 
plasma antibodies			no anti-A or anti-B antibodies	

Figure 1

7. According to **Figure 1**, blood type A would be represented by
   A. group 1
   B. group 2
   C. group 3
   D. group 4

8. Blood group 3 has
   A. no antibodies because you do not produce antibodies against your own antigens.
   B. no antigens because you do not produce antigens against your own antibodies.
   C. no antibodies because you do not produce antigens against your own antibodies.
   D. no antigens because you do not produce antibodies against your own antibodies.

9. NR The following are steps involved in the immune response:

1. Suppressor T cells inhibit the immune system.
2. Antibodies attach to antigens on bacterial cells.
3. B cells produce antibodies.
4. Bacterial cells enter the body and are engulfed by macrophages.

Give the numbers of the steps in the order that they occur, from first to last. (Record all four digits of your answer.)

Part 2

10. (a) **Sketch** an antibody, showing how it attaches to specific antigens.
(b) Label the receptor sites on the cell membrane.
(c) Use the diagram to **explain why** an antibody produced in response to the mumps virus would have no effect against influenza.
(d) Use the diagram to **explain** how antibodies target antigens for phagocytosis.

11. **Explain why** the second time an organism invades the body, the person is not likely to get seriously ill.

12. **Distinguish** between T cell lymphocytes and B cell lymphocytes.

13. **How** do viruses use the receptor sites to gain access into the cell?

14. **Explain why** T cells have difficulty identifying antigens from HIV.

15. **Describe** the function of lymphokine.

16. **Describe** in your own words the function of each of the following:
(a) killer T cells
(b) helper T cells
(c) suppressor T cells
(d) memory B cells

17. **Explain why** the Hawaiian population was so severely affected by measles and the Aboriginal population of North America was so much more susceptible to smallpox than Europeans were.

18. **Define** pluripotent cells.

19. **Why** does the likelihood of autoimmune disease increase with age?

20. **Explain** how a food allergy can threaten life.

Use the following information to answer questions 21 to 23.

The data in **Table 2** were collected from three patients.

Table 2 Blood Cell Counts and Temperature of Three Patients

Patient	Red blood cell count (cells/μL)	White blood cell count (cells/μL)	Body temperature (°C)
normal	5.0×10^6	7 000	37.0
X	2.0×10^6	3 000	37.0
Y	2.5×10^6	10 000	36.5
Z	5.1×10^6	15 000	39.0

21. DE Lead poisoning is characterized by a destruction of bone marrow. Which patient would you suspect has lead poisoning? **Justify** your choice.

22. DE **Predict** which patient has a viral infection. Explain your answer.

23. DE Leukemia is a cancer characterized by the proliferation of white blood cells. Which patient would you suspect has leukemia? **Justify** your choice.

Use the following information to answer questions 24 and 25.

Before the work of Dr. Barry J. Marshall and Dr. Robert Warren of Perth, Australia, most doctors believed that stress was the cause of ulcers. In 1983, Marshall and Warren reported that *Helicobacter pylori*, a bacterium living in the stomach, is the most common cause of ulcers. Today, researchers around the world are turning to another bacterium, *Chlamydia pneumonia*, as the main culprit in triggering coronary heart disease.

24. DE If coronary heart disease is caused by a bacterium, **how** might this affect the search for treatment?

25. DE **Explain why** physicians attempting to diagnose coronary heart disease may be monitoring antibodies.